

II. REMARKS

A. Status of the Claims

Claims 1-14 were pending in the case at the time of the Office Action, with claims 10-14 having been previously withdrawn from consideration. Claims 1 and 2 have been amended in the Amendment set forth herein. Claim 3 has been canceled without prejudice or disclaimer. New claim 15 has been added. Support for the amendments of claims 1 and 2 is discussed below. Thus, claims 1-2, 4-9, and 15 are currently under consideration.

B. Restriction Requirement

Applicants affirm their election, without traverse, of the Group I invention and SEQ ID NOs: 1, 3, 5, 9, 11, 15, 17, 19, 25 and 27 as per the response to Restriction Requirement filed on October 31, 2008. Applicants understand that claims 1-9 are under consideration to the extent that the MUC1-EC polypeptide of the MUC1-EC-human Fc chimeric protein comprises the sequence of SEQ ID NOs: 1, 3, 5, 9, 11, 15, 17, 19, 25, or 27.

C. Sequence Requirements

The specification has been objected to for failing to recite a sequence identifier in association with the sequence recited at page 5, line 22 of the specification. The specification has been amended to recite a sequence identifier in the Amendment set forth herein. Applicants file concurrently herewith a replacement sequence listing.

D. The Claim Rejections Under 35 U.S.C. §102 Are Overcome

Claims 1, 3, 8, and 9 are rejected under 35 U.S.C. §102(e) as being anticipated by Holgersson *et al.* (WO 04/15057; hereinafter "Holgersson"). Holgersson is said to teach fusion proteins that include the same structural and functional properties of those of the aforementioned claims (fusion of MUC1-EC with an Fc polypeptide). Applicants respectfully traverse.

In view of the cancellation of claim 3 without prejudice or disclaimer, the only claims at issue in this rejection include claims 1, 8, and 9.

Without conceding that the claims as originally written would have been anticipated by Holgersson, Applicants note that claim 1, the only independent claim, has been amended to recite the limitation “wherein said first polypeptide sequence is a MUC1-EC polypeptide *wherein amino terminal tandem repeat sequences of MUC1-EC are deleted.*” (emphasis added). Support for this phrase can be found, for example, on page 5, lines 16-27. Claim 2 has been amended to omit those sequences which recite all or part of the tandem repeat sequence of MUC1-EC.

Holgersson concerns fusion proteins that include a first polypeptide that contains a mucin polypeptide which is a polypeptide having a “mucin domain.” Page 8, line 12. A “mucin polypeptide” is defined as “any glycoprotein characterized by an amino acid sequence substituted with O-glycans.” Page 8, lines 13-15. A mucin domain is said to be rich in the amino acids threonine, serine and proline, wherein the oligosaccharides are linked via N-acetylgalactosamine to the hydroxy amino acids (O-glycans). See page 8, lines 18-20.

The instant specification teaches that the N-terminal ectodomain contains variable numbers of conserved 20 amino acid tandem repeats (VNTR region) that is extensively modified by O-glycosylation. Page 1, lines 10-27. The instant specification provides that MUC1-EC polypeptides may include sequences wherein the tandem repeat sequences of the N-terminal are deleted. See page 5, lines 16-27. Thus, MUC1-EC sequences that exclude the tandem repeat sequences do not include a “mucin domain.”

Because Holgersson does not appear to teach chimeric proteins that do not include a mucin domain, it fails to anticipate instant claim 1 (and claims 8 and 9, which depend from claim 1). New claim 19 would not be anticipated by Holgersson because it depends from claim 2, which is a claim that was not included in this rejection and thus considered novel over Holgersson. Applicants therefore respectfully request that the rejection of the pending claims under 35 U.S.C. §102(e) be withdrawn.

E. The Claim Rejections Under 35 U.S.C. §103(a) Are Overcome

Claims 1-9 are rejected under 35 U.S.C. §103(a) as being unpatentable over Holgersson (WO 04/15057) in view of Capon *et al.* (U.S. Patent 5,116,964; hereinafter “Capon”) and Wreschner *et al.* (WO 96/03502; hereinafter “Wreschner”). The Examiner’s position with respect to the teachings of Holgersson is discussed above. Holgersson is said to not specifically teach wherein the human Fc polypeptide is a human IgG1 or IgG2 polypeptide or wherein the MUC1 chimeric protein is a dimer and the dimer is formed by means of a disulfide bridge between the hinges or wherein the MUC1-EC polypeptide comprises SEQ ID NO:1, 3, 5, 9, 11, 15, 17, 19, 25, or 27. The Examiner argues that these deficiencies are made up by the teachings of Capon and Wreschner. Applicants respectfully traverse.

There is no *prima facie* case of obviousness based on Holgersson in view of Capon and Wreschner. As discussed above, Holgersson does not teach or suggest chimeric proteins that include a MUC1-EC sequence that does not include a mucin domain (that is, the tandem repeat sequence at the amino terminal of MUC1-EC). Holgersson emphasizes the importance of mucin domains, noting that its “invention provides mucin-immunoglobulin fusion proteins (referred to herein as ‘αGal fusion proteins’) containing multiple αGal epitopes that are useful as an absorber for anti-αGal antibodies” and that “the αGal fusion proteins are useful in eliminating recipient

anti- α Gal antibodies from blood or plasma prior to a xenotransplantation.” Page 7, lines 27-32. The α Gal fusion protein of Holgersson includes at least one portion of a mucin domain (e.g., O-linked glycosylation site). Holgersson does not appear to teach or suggest inclusion of a mucin protein that does not include a mucin domain, given that mucin domains appear to be critical to its invention.

Further, neither Capon nor Wreschner appear to provide for the missing motivation to provide for the chimeric polypeptides as set forth in the instant claims. Capon is cited as teaching hybrid immunoglobulins that include a ligand binding domain fused to the Fc region to prolong the half-life of the ligand binding domain. Wreschner is only cited as teaching the MUC1 extracellular domain and certain sequences of the MUC1 extracellular domain. Neither reference appears to provide any teaching or suggestion to provide for substituting the mucin domain-containing polypeptides of Holgersson with MUC1 polypeptides that do not include a mucin domain.

Even if one of ordinary skill in the field of the invention had included a MUC1-EC polypeptide excluding a mucin domain in the chimeric polypeptide of Holgersson, there is no reasonable expectation that such a polypeptide would function as an absorber for anti- α Gal antibodies (Holgersson’s goal). To the extent that Holgersson requires presence of a “mucin domain” (*i.e.*, tandem repeat of MUC1-EC), it actually teaches away from the present invention.

In its recent decision addressing the issue of obviousness, *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q.2d 1385 (2007), the Supreme Court stated that in setting forth a *prima facie* case of obviousness, it is necessary to show “some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.”

KSR, 127 S.Ct. 1727 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). In the instant case, Applicants do not identify any rational basis for modifying the teachings of Holgersson to lead to the claimed invention, nor has any such basis been set forth by the Examiner to provide for any chimeric polypeptide that falls within the scope of the pending claims.

Further, is no *prima facie* case of obviousness as to claim 2 for the reasons discussed above. Claim 2 recites SEQ ID NO:19, which is one of the sequences recited in instant claim 2.

In view of the foregoing, it is respectfully submitted that the rejection of claims 1-9 under 35 U.S.C. §103(a) based on Holgersson in view of Capon and Wreschner be withdrawn.

F. Conclusion

In view of the foregoing, it is respectfully submitted that each of the pending claims is in condition for allowance. The Examiner is invited to contact the undersigned attorney at (512) 536-5639 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: June 23, 2009